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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/940,544	09/30/1997	MICHEL SADELAIN	MSK.P-035-US	5042

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EXAMINER
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ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/940,544	Applicant(s) SADELAIN ET AL.	
	Examiner Larry R. Helms	Art Unit 1642	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *24* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Receipt is acknowledged of the request for a Continued Prosecution Application (CPA) filed on 10/01/01 under 37 CFR 1.53(d) based on Application No. 08/940,544. However, it is noted that this application has had one CPA, filed 3/19/01, after the 5/29/00 date and as such the Office has treated the CPA request filed 10/01/01 as an RCE (see 37 CFR 1.114.

The RCE has been entered and claims 1-20 are pending and claims 1-7 are currently under prosecution. An action on the RCE follows.

2. Claims 8-20 are withdrawn from consideration.

Claims 1-7 are under examination.

3. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

4. The following Office Action contains some NEW GROUNDS of rejection.

Rejection Withdrawn

5. The rejection of claims 1-7 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 09/142974 in view of Alvarez-Vallina et al and Sambrook et al is withdrawn.

6. The rejection of claims 1-7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 09/142974 in view of Eshhar et al (WO 93/19163, published 9/30/93), Fouser et al (WO 92/18629, published 10/29/92) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989) is withdrawn.

Response to Arguments

7. The rejection of claims 1-7 under 35 U.S.C. 103(a) as being unpatentable over Cheung et al et al (WO 97/34634, published 9/25/97, Information Disclosure Statement filed 6/3/98), and further in view of Alvarez-Villina et al (Eur. J. Immunol. (1996) 26:2304-209, Information Disclosure Statement filed 6/3/98) and Sambrook et al (Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory, 1989) is maintained for reasons of record.

The response filed 3/25/02 has been carefully considured but is deemed not to be persuasive. The response relies on a declaration by Mr. Sadelain. The declaration has been carefully considured but id deemed not to be persuasive because all of the inventors did not sign the 1.131 declaration as required (see MPEP 715.04). It is noted that the declaration would be persuasive if all applicants sign.

8. The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Cheung et al and further in view of Alvarez-Vallina et al is maintained for reasons of record.

The response filed 3/25/02 has been carefully considured but is deemed not to be persuasive. The response relies on a declaration by Mr. Sadelain. The declaration has been carefully considured but id deemed not to be persuasive because all of the inventors did not sign the 1.131 declaration as required (see MPEP 715.04). It is noted that the declaration would be persuasive if all applicants sign.

9. The rejection of claims 1-2 under 35 U.S.C. 102(a) as being anticipated by Alvarez-Vallina et al (Eur. J. Immunol. (10/1996) 26, pp 2304-2309, Information Disclosure Statement, filed 6/3/98) is maintained for reasons of record.

The response filed 3/25/02 has been carefully considured but is deemed not to be persuasive. The response relies on a declaration by Mr. Sadelain. The declaration has been carefully considured but id deemed not to be persuasive because all of the inventors did not sign the 1.131 declaration as required (see MPEP 715.04). It is noted that the declaration would be persuasive if all applicants sign.

10. The rejection of claims 1-2 under 35 U.S.C. 102(b) as being anticipated by Eshhar et al (WO 93/19163, published 9/30/93) is maintained.

The response filed 3/15/02 has been carefully considured but is deemed not to be persuasive. The response states that the reference is not enabled and does not place it in position of a person of ordinary skill in the field (see page 2-3 of response) and without making such fusion proteins one could not know if the fusion protein that expressed CD28 would function as native CD28 (see page 3). In response to these arguments, Eshhar clearly teaches fusion proteins with an antibody and CD28 (see

page 7-8). In addition, Eshhar et al teach fusion proteins of SCFv-CD16 that are functional and it was routine in the art at the time of the claimed invention to produce fusion proteins and as taught by Eshhar the ScFv-CD16 was functional.

11. The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al (WO 93/19163, published 9/30/93) and further in view of Fouser et al (WO 92/18629) is maintained.

The response filed 3/15/02 has been carefully considured but is deemed not to be persuasive. The response states that applicants point out that the claims are directed to compositions and it appears that the Examiner has found it obvious from a combination of references with a methodology which might be tried and the rejection is akin to that which was reversed in In re Katz, 201 USPQ 71 (CCPA 1979) (see page 3 of response). In response to these arguments, the examiner realizes that which is claimed are products. Knowing that in vitro studies showed that monoclonal antibodies against GD2 and GD3 potentiate lymphocyte response provides motivation to produce an anti-GD2 antibody for tumor and in view of Eshhar who teaches fusion proteins with CD28 it would be obvious to produce the claimed polynucleotide. It is not clear how this is a reverse of In re Katz. In addition, the response states that Fouser provides no more certainty and does not provide any teachings of fusion proteins. In response to this argument, Fouser et al teach the recombinant antibody can be efficaciously combined with recombinant cytokines and in view of Eshhar's teaching one of skill in the art would

combine the antibody and the cytokine of CD28 in a fusion protein because similar fusion proteins have worked (see ScFv-CD16).

12. The rejection of claims 1-7 under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al (WO 93/19163, published 9/30/93) and further in view of Fouser et al (WO 92/18629, published 10/29/92) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989) is maintained.
The response filed 3/15/02 has been carefully considured but is deemed not to be persuasive. The response argues the same points as above and the same response applies.

The following are some NEW GROUNDS of rejection

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

14. Claims 1-2 are rejected under 35 U.S.C. 102(e) as being anticipated by Roberts (U.S. Patent 5,686,281, filed 5/1995, IDS #24)

The claims recite a recombinant polynucleotide encoding a single-chain antibody, a signaling domain of human CD28 receptor and a human CD28 transmembrane domain disposed between the single-chain and the signaling domain.

Roberts teach polynucleotides that encode human CD28 cytoplasmic and transmembrane domains fused to a single-chain antibody (see column 6, lines 55-67).

Claim Rejections - 35 USC § 103

15. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts (U.S. Patent 5,686,281, filed 5/1995, IDS #24) as applied to claims 1-2 above, and further in view of Fouser et al (WO 92/18629, published 10/92) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989).

Claims 1-2 have been described supra. Claims 3-7 recite an antibody that is anti-GD2 and a recombinant polynucleotide further comprising thymidine kinase.

Roberts has been described supra. Roberts does not teach the anti-GD2 antibody or the thymidine kinase.. These deficiencies are made up for in the teachings of Fouser and Sambrook et al.

Fouser et al teach an anti-GD2 antibody and DNA encoding such. Fouser et al also teach the anti-GD2 antibody can be used synergistically with lymphokines, cytokines, etc, to act more efficiently to kill the targeted tumor cells (see page 7).

Sambrook et al teach the thymidine kinase gene, which is expressed in most mammalian cells (Page 16.9). Sambrook et al also teach a plasmid, pTK2, which carries a fragment of the herpes simplex virus (HSV) encoding thymidine kinase (tk) (see page 16.11, Figure 16.1A).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a polynucleotide encoding a fusion protein comprising a single chain anti-GD2 antibody and a signaling domain of human CD28 and human CD 28 transmembrane domain and a gene coding for thymidine kinase.

One of ordinary skill in the art would have been motivated to produce a polynucleotide encoding a fusion protein comprising a single chain anti-GD2 antibody and a signaling domain of human CD28 and human CD 28 transmembrane domain and a gene coding for thymidine kinase because Roberts teach the extracellular domain can be single-chain antibodies and the co-stimulatory signal can be regulated by adding a ligand that binds to the extracellular domain (see column 7, lines 10-21) and in particular the extracellular domain is a single-chain antibody (see column 9, lines 32-52) and the extracellular domain can target tumor cells (see column 10, lines 10-31). In addition, one of ordinary skill in the art would have been motivated to produce a polynucleotide encoding a fusion protein comprising a single chain anti-GD2 antibody and a signaling domain of human CD28 and human CD 28 transmembrane domain and a gene coding for thymidine kinase because Fouser et al teach "The 3F8-type antibodies of the present invention mediate the in vitro cytotoxicity of the target cells that

express the GD2 antigen on the surface (see page 5) and Fouser et al also teach the anti-GD2 antibody can be used synergistically with lymphokines, cytokines, etc, to act more efficiently to kill the targeted tumor cells (see page 7). In addition, one of ordinary skill in the art would have been motivated to produce a polynucleotide encoding a fusion protein comprising a single chain anti-GD2 antibody and a signaling domain of human CD28 and human CD 28 transmembrane domain and a gene coding for thymidine kinase because Sambrook et al teach a medium containing hypoxanthine, aminopterin, and thymidine (HAT medium) "in which only cells expressing the tk gene will grow. Thus, by using the appropriate medium it is therefore possible to select for cells expressing the tk gene". Thus, it would have been obvious to combine the teaching of Roberts and Fouser et al for producing a polynucleotide encoding for a fusion protein of a single chain anti-GD2 antibody and the signaling and transmembrane domains of CD28 and further combine this polynucleotide with a polynucleotide encoding the thymidine kinase protein of Sambrook et al for selection of cells expressing the polypeptide.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art a the time the invention was made, as evidenced by the references.

Conclusions

16 No Claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

Sheela J. Huff
SHEELA HUFF
PRIMARY EXAMINER